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Confidential Time and Extent Application for Climbazole
(INCI: Climbazole)
Trade Name: Crinipan® AD

§330.14 (b) (1)

Climbazole is sold in more than 70 countries in the world as an anti-dandruff agent. It is not sold anywhere in the world, that we know of, where the product requires a prescription, or is restricted to pharmacy only sales, “under-the-counter” sales or any other restrictions. It was first used as the active ingredient in anti-dandruff agents in 1998 and has enjoyed continuous sale since then.

§330.14 (b) (2)

Climbazole has been sold continuously for the past 5 years in the following countries: Brazil, France, Germany, Great Britain, Mexico and Spain.

§ 330.14 (c) (1)

Basic information describing the new condition as well as information requested according to 330.14 (c) (1) (i) are included in table 1 below. As Climbazole is not a botanical drug substance its information according to 330.14 (c) (1)(ii) not applicable.

Table 1

Active ingredient or botanical drug substance	Climbazole
Pharmacological class	Climbazole is a conazole fungicide
Intended OTC use	Use in shampoo and cleaner as an anti-dandruff agent.
Strength	Climbazole Leave-on: 0.1 – 0.5% Rinse off. 0.5 – 2.0%
Dosage form	Shampoos, conditioners, creams, lotions and tonics
Route of Administration	Topical
Directions for use	Please refer to the labelling and Patient
Current OTC monograph under which the condition would be marketed or request and rationale for creation of a new OTC drug monograph	Dandruff, Seborrheic Dermatitis, and Psoriasis Drug Products for Over-the-Counter Human Use; Final Monograph 12/4/1991 (21 CFR part 358, subpart H)
Active Ingredient Description	
Chemical and physical	Chemical name: 1-(4-chlorophenoxy)-1-(imidazole-1-yl)-

characteristics	3,3-dimethyl-butanone. Off-white to pale brownish crystalline powder. Mp 98 – 99°C. Virtually insoluble in water. Readily soluble in solvents such as benzyl alcohol, ethanol and phenoxyethanol.
Method of synthesis or isolation	See appendix 1
Method of purification	The crude climbazole is recrystallised from toluene.
Additional specifications or analytical methods	Reference is given to the USP/NF monograph proposal.
References to USP-NF or foreign compendia	Submitted to the USP. USAN name: Climbazole. No foreign compendia

§ 330.14 (c) (2)

Please refer to § 330.14 (c) (4) below for the major markets. A total listing of all countries with the kilos of active ingredient sold per year is attached as appendix 2.

§ 330.14 (c) (3)

For the countries where Climbazole containing products has been marketed for more than 5 continuous years (see § 330.14 (c) (4) product labelling with English translations for the following products are provided as listed in Table 2.

Table 2

Country	Manufacturer, Product	Appendix
Brazil	<ul style="list-style-type: none"> Colgate Palmolive, Palmolive Naturals Condicionador Colgate Palmolive, Naturals Shampoo 	3
Germany	<ul style="list-style-type: none"> Wella, Crisan Anti-Schuppen Shampoo Jeder Haartyp Wella, Crisan Anti-Schuppen Shampoo Normales Haar Wella, Crisan Anti-Schuppen Shampoo Fettiges Haar Wella, Crisan Anti-Schuppen Shampoo Kraft und Stärkung für Dünnes Haar Wella, Crisan Anti-Schuppen Shampoo Intensiv Wella, Lifetex balanced active Shampoo Schwarzkopf, Seborin Regulativ Shampoo Vorbeugend u. Mild Schwarzkopf, Seborin Intensive Shampoo Hochwirksam Colgate-Palmolive, Palmolive Gard Pflege-Shampoo Extra Control E. Kissing GmbH, Kür Pflege Shampoo Anti-Schuppen Sebaharma, Sebamed Antischuppen Shampoo 	4

	<ul style="list-style-type: none"> • Beiersdorf, Eucerin Antischuppen Shampoo • Boots Healthcare, Balneum Aqueo Shampoo 	
Spain	<ul style="list-style-type: none"> • Wella, Wella Balsam Campu • Wella, System Professional Remove Shampeeling • Wella, System Professional Remove Shampoo • Wella, System Professional Removing Intensive Shampoo • Wella, Lifetex Balanced Care Tónico Control • Myrugia S.A. Lactovit champu nutritivo (Nuevo) 	5
France	<ul style="list-style-type: none"> • Laboratories Biorga, Squapane E Shampooing Antipelliculaire D'entretien • Laboratories Biorga, Squapane P Shampooing Keratoregulateur • Laboratories Biorga, Squapane P Shampooing Keratoregulateur Forte • Boots Healthcare, Balneum Aqueo Shampooing • Schwarzkopf, Seborin Intensive Shampoo Anti-Pelliculaire 	6
Great Britain	<ul style="list-style-type: none"> • Wella, Vosene Light and Gentle Conditioner • Wella, Vosene Original Shampoo • Colgate Palmolive, Palmolive Naturals Shampoo Extra Control • Neutrogena Corp., Neutrogena Shampoo Healthy Scalp 	7
Mexico	<ul style="list-style-type: none"> • Wella, Crisan Shampoo Anti-Caspa Intensivo 	8

§ 330.14 (c) (4)

The information describing marketing experience by country is provided in accordance with § 330.14 (c) (4) as Climbazole has been marketed OTC in five or more countries with a minimum of 5 continuous years of marketing in at least one country. The product information is provided on the following countries: Brazil, France, Germany, Great Britain, Mexico and Spain. This information is provided in table 3-1 to 3-6 below.

The cumulative total number of dosages for each country is calculated by dividing the total weight of the active ingredient sold by the total weight of the active ingredient in the largest pack size sold. The content of Climbazole is typically 0.7%. The accumulated sales include data from 1999 until June 2004.

The information on demographics is sourced from the CIA website.

The demographics for the individual countries show a large variability. However, this has not given rise to any particular pattern in the user characteristics, labelled use pattern or in the labeling information for the products marketed in the individual countries.

The demographics for The US is given as white 77.1%, black 12.9%, Asian 4.2%, American and Alaska native 1.5%, native Hawaiian and other pacific Islander 0.3%, other 4%. This does not give rise to any special concern as the US demographic is not more extreme diverse than any of the countries where the product has been marketed for 5 years or more, and where special warnings or considerations have not been issued.

Table 3-1

Country	Brazil
Marketing status (if limited to pharmacy sale, list reason why and collateral measures)	Direct to consumers.
Length of the current marketing status	Continuously since 1998.
Population demographics	White 55%, mixed white and black, black 6%, other 1%.
Cumulative total number of dosage units sold for each dosage form	[REDACTED]
Labeled use pattern, as applicable	No limitation to use. Apply and rinse after a few minutes.
System for identifying adverse drug experiences (ADRs)	Drugs and Cosmetics registration in Brazil is imposed and controlled by the National Health Administration Agency – Agência Nacional de Vigilância Sanitária, usually referred as ANVISA, created in 1999. The agency has enforcement powers similar to FDA, including cancellation of permit trade for drugs, food, medical and cosmetic products and licensing of manufacturers and distributors. No product without clinically or therapeutically proven beneficial substance in its formula, can be registered with the ANVISA; The norms and procedures required to register hygiene products, cosmetics and toiletries or to modify an existing registration are defined in Resolution 78, August 28th, 2000. This resolution was published to update the Brazilian Law 6360 of 1976 and its addition number 74.094 of 1977 and Administrative Act number 71/96.

Table 3-2

Country	Germany
Marketing status (if limited to pharmacy sale, list reason why and collateral measures)	Direct to consumers.
Length of the current marketing status	Continuously since 1999.
Population demographics	White 91.5%, Turkish 2.4%, other 6.1%.

Cumulative total number of dosage units sold for each dosage form	[REDACTED]
Labeled use pattern, as applicable	Daily or regular use. Allow to work for 2 – 3 minutes, then rinse carefully.
System for identifying adverse drug experiences (ADRs)	There is a product register according to EU legislation and all adverse reactions are required to be reported in the company's product information package. This package must be made available to the competent authorities.

Table 3-3

Country	Spain
Marketing status (if limited to pharmacy sale, list reason why and collateral measures)	Direct to consumers.
Length of the current marketing status	Continuously since 1999.
Population demographics	Not disclosed.
Cumulative total number of dosage units sold for each dosage form	[REDACTED]
Labeled use pattern, as applicable	Use for 4 weeks, 3 times a week. Apply for 2 minutes and rinse carefully.
System for identifying adverse drug experiences (ADRs)	There is a product register according to EU legislation and all adverse reactions are required to be reported in the company's product information package. This package must be made available to the competent authorities.

Table 3-4

Country	France
Marketing status (if limited to pharmacy sale, list reason why and collateral measures)	Direct to consumers.
Length of the current marketing status	Continuously since 1999.
Population demographics	Not disclosed.
Cumulative total number of dosage units sold for each dosage form	[REDACTED]
Labeled use pattern, as applicable	2 to 3 times per week without restriction in duration. Apply for 2 – 3 minutes, rinse carefully. Avoid contact with the eye.
System for identifying adverse drug experiences (ADRs)	There is a product register according to EU legislation and all adverse reactions are required to be reported in the company's product information package. This package must be made available to the competent authorities.

Table 3-5

Country	Great Britain
Marketing status (if limited to pharmacy sale, list reason why and collateral measures)	Direct to consumers.
Length of the current marketing status	Continuously since 1999.
Population demographics	White 97.2 %, other 2.8%.
Cumulative total number of dosage units sold for each dosage form	[REDACTED]
Labeled use pattern, as applicable	No limitations in use. Apply for 1 - 2 minutes, rinse carefully.
System for identifying adverse drug experiences (ADRs)	There is a product register according to EU legislation and all adverse reactions are required to be reported in the company's product information package. This package must be made available to the competent authorities.

Table 3-6

Country	Mexico
Marketing status (if limited to pharmacy sale, list reason why and collateral measures)	Direct to consumers.
Length of the current marketing status	Continuously since 2000.
Population demographics	Mestizo (Amerindian-Spanish) 60%, Amerindian or predominantly Ameridian 30%, white 9%, other 1%.
Cumulative total number of dosage units sold for each dosage form	[REDACTED]
Labeled use pattern, as applicable	No limitations in use. Apply and rinse carefully with water.
System for identifying adverse drug experiences (ADRs)	The MOH and specifically the Direccion General de Medicamentos y Tecnologías para la Salud has a National Center for Pharmacovigilance (CNFV) in charge of receiving, recoding and evaluating ADRs by pharmaceutical products dispensed in Mexico with or without prescription. The legal basis for the "Pharmacovigilance permanent program" (PPP) is established in the Rules of the General Law of Health: Art. 58 - V bis. (May, 7 1997), Section five, Art. 38. and Title five Art. 131 Chapter 1. (Feb. 4 1998).

Table 7-3. Time and Extent of Climbazole Marketing in 3 Regions During 1999-2004

Country	Marketing Extent (dosage units x 10⁶)
Europe	62.8
North America	30.9
South America	17.2
TOTAL	110.9

There are no countries where climbazole containing products are prescription only.

§ 330.14 (c) (6)

To the best of our knowledge there are no cases where climbazole containing products have been withdrawn from the market for other than commercial reasons and likewise there are no countries known to the sponsor where an approval of OTC status has been denied.

§ 330.14 (c) (7)

The request to provide the summarized data in tabular format is fulfilled by the above tables.

§ 330.14 (c) (8)

Not applicable as the product is not marketed in the US.